REMARKS

The above-captioned patent application has been carefully reviewed in light of the non-final Office Action to which this Amendment is responsive. Claims 1-3, 7-9, 23 and 34 have been amended in an effort to more clearly define and particularly point out that which is regarded as the present invention. Claims 12-16 and 20-22 have been canceled. No new matter has been added to the above-captioned application.

The Examiner has rejected all pending claims on the basis of certain prior art, particularly Killeen et al. (U.S. Patent No. 5,166,051), either taken alone or in combination with either Fruitstone et al. (U.S. Patent No. 4,259,057), Cremins et al. (U.S. Patent No. 4,978,624) or Maimon, et al. (U.S. Patent No. 5,350,693). Claims 1-11 further stand provisionally rejected under the doctrine of obviousness type double patenting over Claims 1-19 of USSN 10/398,711. Claims 1-16, 20, 20-27 and 31-34 have also been rejected based on 35 USC §112, second paragraph.

Applicants respectfully requests reconsideration of the claimed subject matter and withdrawal of all objections based on the amended and canceled claims and the following comments.

Turning first to the prior art rejections, the Examiner has rejected Claims 1-4, 7-14, 21-25 and 31-34 under 35 USC §102(b) as being anticipated by Killeen et al. (U.S. Patent No. 5,166,051).

Applicants respectfully traverse this rejection. In order to successfully anticipate under the Statute, each and every claimed limitation must be found, or its structural equivalent, in the single cited reference.

The present invention is characterized in that in a liquid specimen comprising cell components being mixed, the cell components in the liquid specimen are shrunk by a cell shrinkage reagent provided on a carrier of a biosensor and the liquid specimen are developed toward a reaction layer of the carrier that is provided chromatographically downstream in a state the shrunk cell components being mixed in the liquid specimen.

To the contrary, as explained in the response to the first Office Action, the biosensor disclosed in Killeen screens components in the blood specimen by minute pores on the membrane, and prevents red blood spheres from moving to the detection zone, thereby providing an effect that is totally different from that of the present invention.

As described in the present application, when components in the blood or other liquid are to be detected employing a conventional chromatography, a method of previously performing centrifugation or previously setting a blood cell filter on the chromatography sensor thereby to filter out the blood sphere components, and then developing the plasma components or serum components were mainly utilized. However, these methods required a large amount of blood for obtaining a required amount of analytes, and it was impossible to carry out an easy and fast measurement.

The present invention was directed to solving the above-described problems and has an object of performing a blood component analysis with a minute amount of analytes, as well as with ease, fast, and high precision. This object is realized by providing a constitution in which a cell shrinkage reagent is provided chromatographically upstream on a biosensor in order to shrink the cell components in the liquid specimen, wherein the shrunk cell components are developed together with the liquid specimen chromatographically downstream along the biosensor.

As indicated by the Examiner, embodiment 2 in the present invention includes the description that the cell components which are shrunk by the textile at the marker reagent holding part are separated at upstream of the reaction area, and those which can perform such separation of cell components are restricted to reaction layer filtering type chromatography sensors.

To the contrary, however, and in the reaction layer horizontal direction developing type chromatography sensor as disclosed in embodiment 1, the shrunk cell components are developed on the reaction layer 4 toward chromatographically downward in the state of being mixed in the liquid specimen. In order to clearly

point out this difference in characteristics, Claims 1 and 23 have been amended to more clearly point out the above salient features as shown in Figs. 1 and 2 and as described, for example, at pages 20-23 of the above-captioned application.

In Killeen, on the other hand, an overlay membrane completely contacts and covers the whole detection layer. This overlay membrane is made of synthetic polymer containing a reagent for shrinkage and solidification. Killeen is characterized in that the overlay membrane contains a reagent for shrinkage and solidification, that the overlay membrane has a constitution of completely contacting and covering the whole detection layer, such that red blood cells in the blood added into the overlay membrane get shrunk and solidified while passing the overlay membrane. These cells are unable to penetrate into the detection layer, thereby enabling a detecting of the blood components without the existence of red blood cell. Therefore, it is readily seen that the object of Killeen is to completely and fully separate the blood sphere components that were conventionally difficult to be detected due to the co-existence of red blood cells, and it is obvious from the foregoing that blood sphere components can never pass the overlay membrane in Killeen.

To the contrary, the present invention is characterized by a biosensor utilizing and related method as recited in Claims 1 and 23, the sensor including a part holding a cell shrinkage reagent is provided chromatographically upstream wherein cell components in the applied liquid specimen are shrunk thereat, and the cell components shrunk thereat are sufficiently developed together with the liquid specimen in a direction chromatographically downstream on the reaction layer without clogging. According to the present invention, easy and quick measurement can be performed with only a minute quantity of blood, and a high-accuracy blood component analysis can be performed easily and quickly without having any special constitution.

Because Killeen fails to describe or suggest the passage of both liquid components and the shrunk cell components downstream from the specimen adding part of the sensor/carrier, there can be no anticipation under the Statute. Reconsideration is respectfully requested. Claims 2-4, 7-11, 24, 25 and 31-34 are believed allowable for the same reasons since these claims depend upon Claims 1 and 23, respectively.

The Examiner has further rejected Claims 5-6, 15-16, 26-27 under USC §103(a) as being unpatentable over Killeen et al. in view of Fruitstone et al. (U.S. Patent No. 4,259,207), Claims 6, 16 and 27 over Killeen et al. in view of Cremins et al. (U.S. Patent No. 4,978,624), and Claim 20 over Killeen et al. in view of Maimon et al. (U.S. Patent No. 5,350,693).

Applicants also respectfully traverse these rejections in toto, though the rejection to Claim 20 over Killeen et al. and Maimon is moot since Claim 20 has been canceled. First and in order to successfully maintain a "*prima facie*" obviousness rejection under the Stature, each and every essential claimed feature or limitation must be found, or its substantial equivalent, in the cited art, either above or in combination. For a combination to exist, there must be motivation found in the prior art as a whole at the time of the invention to one of sufficient skill. The references cannot be combined as a result of impermissible hindsight (i.e., advance knowledge) of the invention.

Killeen has been discussed with regard to the present invention above. As noted therein, this invention is believed to be distinguishable from the cited art in that Killeen fails to describe, suggest or otherwise infer a biosensor and related analytical method in which cell components of a liquid specimen are shrunk on a specimen shrinkage part and wherein shrunk cell components from the applied liquid specimen are carried downstream chromatographically along with the liquid specimen to a reaction layer.

The inclusion of each of the secondary references by the Examiner fail to teach or otherwise disclose the above essential features, now recited in Claims 1 and 23 of the above-captioned application. Therefore, there can be no *prima facie* case

of obviousness under the statute with regard to the dependent claims rejected by the Examiner. Therefore reconsideration of Claims 5, 6, 26 and 27 are respectfully requested. Claims 15, 16 have been canceled.

With regard to the provisional double patenting rejection, Applicants herein attach a Terminal Disclaimer to obviate a provisional double patenting rejection over the pending noted application.

Finally, and regarding the Section 112 rejections under second paragraph, Applicants have amended each of Claims 1, 23 to correct antecedent basis problems and to clarify and distinctly describe the invention. To that end, no new matter has been added. The objections to Claim 12 are moot, in that this claim has been canceled. Claims 2 and 3 have been canceled to clarify the liquid specimen used while Claim 34 has been amended to more clearly specify the concentration range of the cell shrinkage reagent. No new matter has been added.

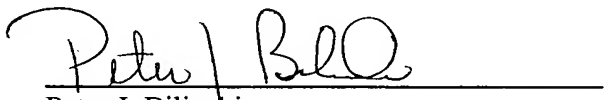
In summary, it is believed the above-captioned patent application is in an allowable condition and such allowance is earnestly solicited.

If the Examiner wishes to expedite disposition of the above-captioned patent application, he is invited to contact Applicant's representative at the telephone number below.

The Director is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. 50-0289.

Respectfully submitted,

WALL MARJAMA & BILINSKI LLP

By: 

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